

**A DOUBLE BLIND RANDOMIZED CONTROL STUDY  
COMPARING THE EFFICACY OF 0.25% ISOBARIC  
BUPIVACAINE TO 0.5% HYPERBARIC BUPIVACAINE  
DURING SPINAL ANAESTHESIA FOR LOWER LIMB  
SURGERY IN ASA II AND ASA III PATIENTS**

A DISSERTATION SUBMITTED IN PART FULFILLMENT  
OF THE REQUIREMENT OF THE Dr. M G R MEDICAL  
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By

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# CERTIFICATE

This is to certify that the work carried out in this thesis entitled ‘A DOUBLE BLIND RANDOMIZED CONTROL STUDY COMPARING THE EFFICACY OF 0.25% ISOBARIC BUPIVACAINE TO 0.5% HYPERBARIC BUPIVACAINE DURING SPINAL ANAESTHESIA FOR LOWER LIMB SURGERY IN ASA II AND ASA III PATIENTS’ was carried out by Dr.Vasudha.B.Rao in the department of Anaesthesia, Christian Medical college, Vellore under my supervision and guidance.

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## AIMS AND OBJECTIVES...

## **Aims and Objectives:**

To compare the efficacy of two solutions of bupivacaine, 1.5ml of 0.5% bupivacaine and 3 ml of 0.25% hyperbaric bupivacaine in providing stable hemodynamics.

To compare the time of onset, height of block, intensity of sensory and motor blockade, duration of analgesia as well as the incidence of side effects between the two groups.

## INTRODUCTION...



Augustus Karl Gustav Bier was the first to introduce cocaine intrathecally in six patients coming for lower limb Surgery in 1898, since then spinal anaesthesia has seen many modifications from the local anesthetics to the spinal needle in use. In the last few decades, the use of regional techniques for anaesthesia and analgesia has significantly risen. This is mainly because of awareness of the benefits of regional anaesthesia particularly in an aging population riddled with a wide range of intercurrent illness.

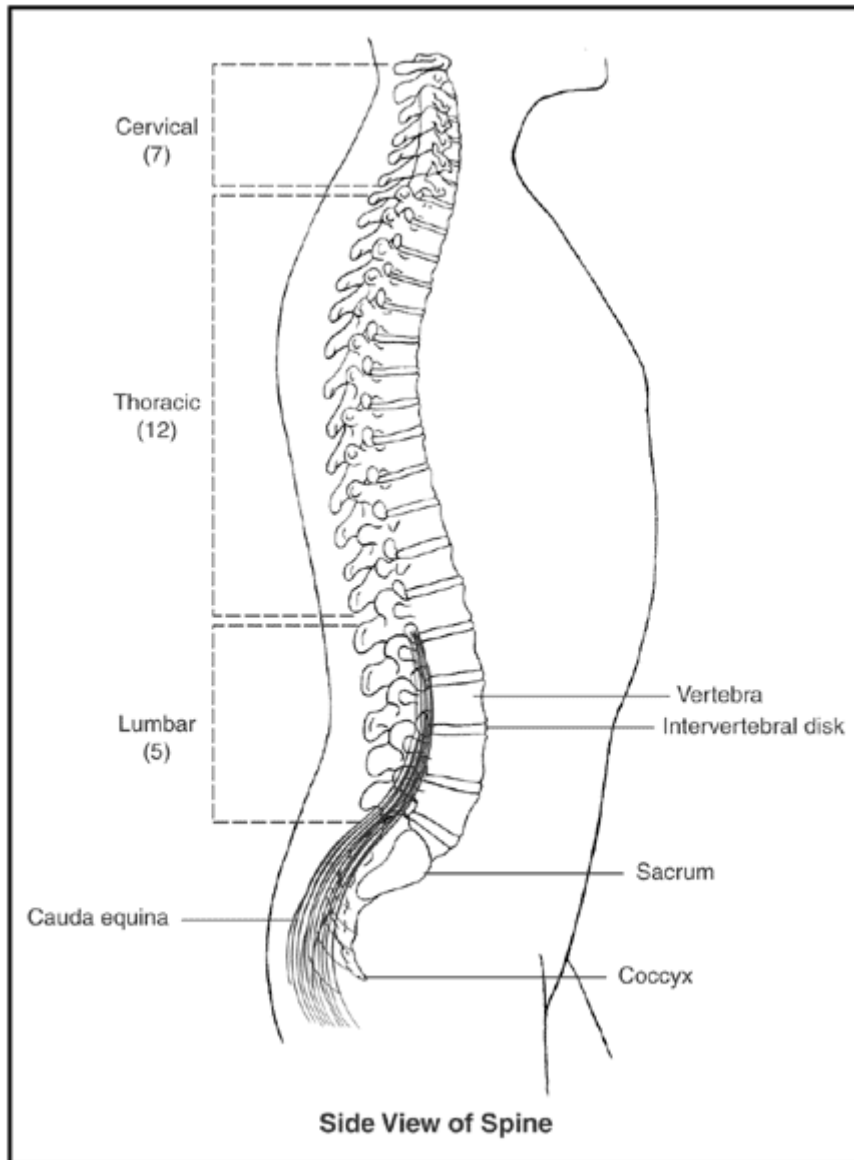
Amongst the various regional techniques, spinal anaesthesia is amongst the most commonly used, besides being easier to perform with definitive results. Though spinal anaesthesia is generally limited for procedures below the umbilicus, its usage has been plentiful. The main advantage of spinal anaesthesia being the ability to control the level of anaesthesia and to a certain extent the duration of anaesthesia by altering the drug characteristics, dosage and patient position during and immediately after the spinal anaesthetic.

The commonly used local anaesthetic for spinal anaesthesia is

hyperbaric bupivacaine, though this gives good motor and sensory block it is associated with hypotension and at times bradycardia which can be detrimental in the elderly and those with intercurrent illnesses like hypertension, diabetes mellitus, ischemic heart disease as hemodynamic instability worsens already compromised organ function in this subset of people. Alteration of the drug characteristics can limit the degree of hemodynamic instability and this is what we aspire to do in this study.

The challenge during a subarachnoid block lies in the ability to provide enough local anaesthetic to provide adequate anaesthesia for surgery while preventing extensive cephalad spread and unwanted adverse effects.

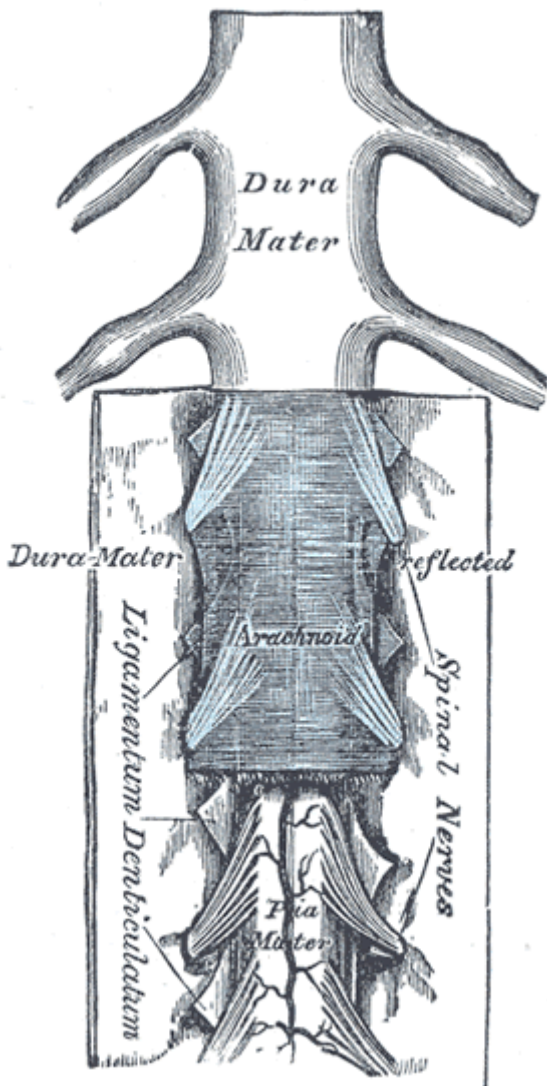
# ANATOMY



Spinal anaesthesia can successfully be used in a number of situations, but in order to conduct a safe procedure, thorough knowledge of the relevant anatomy, pharmacology of local anaesthetics, physiologic effects of spinal anaesthesia, technique and complications is necessary.

There are 33 vertebrae in the spinal column of which 7 are cervical, 12 thoracic, 5 lumbar, 5 sacral and 4 are coccygeal. The vertebral column has the cervical and lumbar curves convex anteriorly, whereas the thoracic and sacral curves are convex posteriorly, this curvature of the spine along with other factors play an important role in determining the extent of spread of the local anaesthetic.

Five ligaments hold the spinal column, of these the supraspinous ligament connect the apices of the spinous processes from C7 to S2, while the interspinous ligament holds the spinous processes together. The ligamentum flavum binds the laminae above and below, while the anterior and posterior ligaments bind the vertebral bodies together.



The spinal cord is 45cm long in the adult. It has an elongated cylindrical shape but flattened antero posteriorly. The spinal cord begins at the foramen magnum and forms the conus medularis below, the filum terminale extends further to get attached to the coccyx. The spinal nerves below the conus medularis form the cauda equina.

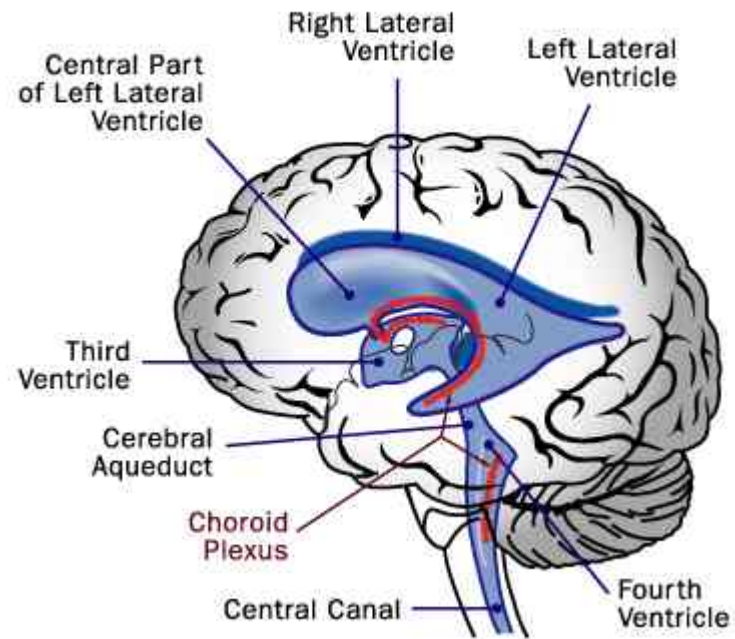
The spinal cord is covered by three meninges: dura, arachnoid and pia mater. The dura is the outermost and a tough layer, while the arachnoids forming the middle layer is a delicate non vascular layer closely attached to the dura. The pia mater is the innermost layer closely investing the spinal cord, it is a highly vascular layer.

There are three compartments closely related to the meninges, these are the epidural, subdural and subarachnoid spaces. The epidural space is outside the dura but within the vertebral canal, its contents are fat, blood vessels, nerve roots and lymphatics, they are not distributed uniformly but appear in compartments. The subdural space is a potential one as the arachnoid membrane is in close contact with the dura separated by a thin film of serous fluid.

The subarachnoid space contains the cerebrospinal fluid and communicates with the tissue spaces around the vessels in the pia mater.

The spinal cord ends at L3 at birth but in adults reaches only up to the lower border of L1. Normally there are 31 pairs of symmetrically arranged spinal nerves attached to the spinal cord by two roots, the anterior and posterior roots. Each nerve is formed by fusion of an anterior and posterior root, immediately distal to this the posterior root carries a ganglion. The anterior roots are motor while the posterior roots are sensory.

## The Ventricular System of the Human Brain



The blood supply comes from the anterior spinal artery which supplies the entire length of the cord in front of the posterior grey column, while the posterior spinal artery supplies the posterior grey and white columns on either side. In many patients an important source of blood supply to the lower half of the spinal cord is from the artery of Adamkiewicz, which is a direct supply from the aorta usually arising at the 11<sup>th</sup> thoracic space. Venous drainage is by a plexus of anterior and posterior spinal veins which eventually drain into the segmental veins that communicates with the medullary vein <sup>1,2,3</sup>.

### **Cerebrospinal Fluid (CSF)**

CSF is formed by the secretory cells of the choroid plexus which is in communication with the lateral, third and fourth ventricle. CSF flows via the third ventricle through the aqueduct and fourth ventricle to enter the subarachnoid space through the two lateral foramen of Luchska and median foramen of Magendie. The total volume of CSF in an adult is about 150ml, produced at the rate of 0.35-0.40 ml/ min or 500-600ml in a day, the turnover time being 5-7hrs. Half of this volume is present intracranially and rest is in the subarachnoid space into which the injected drug gets distributed. <sup>60</sup>

CSF is an isotonic, aqueous medium with a composition similar to interstitial fluid. The density of CSF at 37<sup>0</sup>C has a range of 1.0000-1.0006 with a mean of 1.0003 g/liter. However, in humans CSF density is not uniform and varies with age, sex, pregnancy and illness.<sup>4,5</sup> CSF is not static and continuously oscillates with arterial pulsations, studies have indicated that the extent and duration of spinal anaesthesia with isobaric bupivacaine depend on the CSF velocity. <sup>6</sup>



PHARMACOLOGY OF LOCAL  
ANAESTHETICS

Successful spinal anaesthesia requires a sound knowledge of the pharmacology of local anaesthetics administered in the intrathecal space.

Local anaesthetics act by blocking neuronal conduction. The normal resting membrane potential is -60 to -70 mV resulting from a dynamic balance between ionic concentration gradients maintained by the  $\text{Na}^+/\text{K}^+$  ATPase pump and the diffusion potential of ions, mainly  $\text{Na}^+$  and  $\text{K}^+$ . When an action potential is generated the resting membrane potential reaches threshold potential, resulting from activation of  $\text{Na}^+/\text{K}^+$  ATPase which pumps 3 molecules of  $\text{Na}^+$  extracellularly for 2 molecules of  $\text{K}^+$  intracellularly, creating an electrical field across the cell membrane.<sup>7</sup> The  $\text{Na}^+$  channel exists in three states: closed, active and inactive. Local anaesthetics can block the channel in the active state as  $\text{Na}^+$  conduction occurs only during this state.<sup>8</sup>

Local anesthetic inhibition of  $\text{Na}^+$  currents increases with repetitive depolarizations in a process called phasic block. Phasic block represents increased LA binding, either because more channels become accessible during depolarization or because the channel conformations favored by depolarization bind LA with higher affinity.<sup>9</sup>

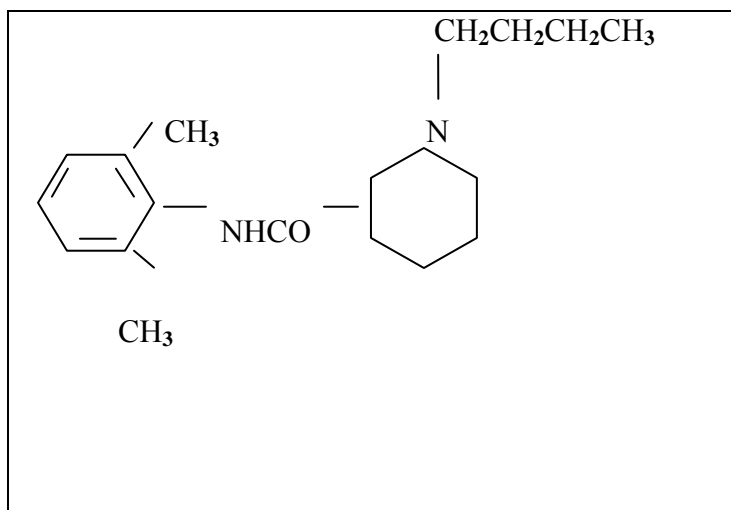
Thus, local anaesthetic solutions cause reversible blockade of impulse propagation in a manner that is both time and voltage dependant, resulting in an increased threshold for activating the action potential.<sup>10</sup> **Anaesthetic potency** The clinically useful local anaesthetics have a lipophilic, substituted benzene ring linked to a hydrophilic amine group via an ester or amide linkage, this linkage results in two chemically distinct groups the aminoamides and the aminoesters.

Local anaesthetic potency, speeds of onset, duration of action is determined by the dissociation constant pKa, lipid solubility and degree of protein binding. <sup>11</sup>

### **BUPIVACAINE – Pharmacology**

Group – Amino amide

Chemistry



Systematic name

(*RS*)-1-butyl-*N*-(2,6-dimethylphenyl) piperidine-2-carboxamide

Chemical data

Formula: C<sub>18</sub>H<sub>28</sub>N<sub>2</sub>O

Molecular weight: 288.43 g/mol

Pharmacokinetic data

pH: 8.1

Protein binding: 95%

Lipid solubility: highly lipid soluble

% ionized at pH 7.4: 83%

Metabolism: Hepatic

Elimination half life: 3.5 hrs

Excretion: Renal

Toxic dose: 2.5-3 mg/Kg

Toxic plasma concentration: >3 mcg/ml

#### Specific features

More cardio toxic than other local anaesthetics

CVS: CNS ratio 2.0 <sup>12</sup>

### **DETERMINANTS OF CLINICAL EFFICACY OF SPINAL ANAESTHESIA**

Distribution of local anaesthetics in the subarachnoid space determines the extent of sensory and motor block, the uptake into neuronal tissues determines which neuronal function is affected while their elimination dictates the duration of action.

A number of factors affect the distribution of local anaesthetics in the subarachnoid space <sup>13</sup>, the most important factor is the baricity of the injected solution, and others are the dose of the local anaesthetic and position of the patient during and just after the spinal block. <sup>13,14,15,16,17,18</sup>

About a decade ago Barker was the first to study the factors affecting intrathecal spread of local anaesthetics, he deduced that gravity and the lumbosacral curves can be used to influence the spread of local anaesthetic made hyperbaric with addition of glucose.<sup>19</sup>

Table 1

**Factors affecting intrathecal spread of local anaesthetics, modified from <sup>31</sup>**

Characteristics of injected solution	Technique	Patient characteristics
Baricity Volume=dose=concentration Temperature of injectate Viscosity Additives	Patient position Level of injection Needle type=alignment Intrathecal catheters Fluid currents Epidural injection	Age Height Weight Sex Intra-abdominal pressure Spinal anatomy Lumbosacral cerebrospinal fluid volume Pregnancy

**Baricity**

It is the density of the local anaesthetic to the density of CSF at 37o C, it is this factor that determines the spread of the local anaesthetic in the subarachnoid space. Hypobaric local anaesthetic has a lesser density than CSF and hence tends to rise against gravity isobaric solutions have a similar density to CSF thereby get distributed around the site of injection, gravity ideally does not affect its spread.

On the other hand a hyperbaric solution is denser than CSF and tends to follow gravity. As these local anaesthetics depend on gravity to determine the extent of spread, it goes without saying that the patient's position immediately after a spinal block determines the point of gravity, thereby affecting the spread of the anaesthetic.

Hyperbaric solutions have a more predictable spread but to high levels of blockade can have detrimental cardio respiratory effects, on the other hand plain solutions commonly are unpredictable in their extent of spread.<sup>20, 21.</sup> The average specific gravity of CSF is 1.0069. The baricity of the study drug (1.5ml of 0.5% bupivacaine + 1.5ml of sterile saline) estimated in our hospital was found to be 1.0061.

### **Volume/dose/concentration injected**

It is impractical to change one factor without changing the other, hence studies trying to determine the role of each factor are difficult to perform, nevertheless most studies attempting this have shown that drug dose to be more important.<sup>22,23,24,25</sup>

### **Temperature of injectate**

The baricity may change slightly with different temperature, even this small change can make a hypobaric solution hyperbaric or vice versa. Local anaesthetics are injected into the CSF at room temperature (~24oc) when it enters the CSF there might be a local drop in Temperature which recovers quickly, the injected solution is then at body temperature and might behave differently than expected due to changes in baricity.<sup>26</sup>

## **CLINICAL TECHNIQUE**

### **Patient position**

The interplay between density and patient position due to the effects of gravity makes posture an important determinant in deciding the extent of spinal block. True isobaric solutions should ideally not be affected by patient posture.

### **Level of injection**

Greater level of cephalad spread is seen when a higher level of injection is given with plain solutions, this finding is however less consistent with hyperbaric solutions.<sup>27,28,29</sup>

## **PATIENT CHARACTERISTICS**

### **Age, height, weight, sex**

At the extremes of age there are small but significant increases in maximum spread, rate of onset of motor block and cardiovascular instability, regardless of the solution used. It is probable that these are secondary to age-related changes in spinal anatomy, nerve physiology and cardiovascular reflexes.<sup>30</sup> Increased body mass index has shown to result in a higher cephalad spread of local anaesthetic, the epidural fat is considered to compress the dural sac, decrease the CSF volume resulting in an increased spread. Gender has no role to play in the spread of local anaesthetics.<sup>31</sup>

## **ASSESSMENT OF SPINAL BLOCK**

There are numerous studies attempting to study the factors affecting the intrathecal spread of local anaesthetic in the CSF to use these in the clinical setting will be impractical. There are

indirect measures by which degree or height of spinal block can be measured. This is done by assessing for loss of sensory, motor and autonomic function which are blocked by spinal anaesthesia. There are various types of nerve fibers, each of which have different features. The preganglionic B fibers carry autonomic impulses while the C fibers carry post ganglionic sympathetic nerve fibers, both of these are more sensitive to blockade by local anesthetic than the A fibers.

The A fibers are further divided into  $\alpha$ ,  $\beta$ ,  $\lambda$ ,  $\delta$ , which carry proprioception, touch pressure, light touch and motor fibers respectively, of these A  $\lambda$  are largest in diameter and are more difficult to block. The variation in response to local anaesthetics results in a differential blockade, clinically this translates as different levels of neural blockade, autonomic nerves are blocked at a higher level than sensory which in turn is blocked at a higher level than motor, these are generally separated by two or more segments. In practice, height of block starting from a non anaesthetised area is checked for temperature (response to cold), pinprick, while motor block is assessed by using modified Bromage scale as follows:

Grade	Definition
0	No motor block Inability to raise extended leg; able to move knees and feet
1	Inability to raise extended leg and move knee; able to move feet
2	
3	Complete block of motor limb



## **PHYSIOLOGIC EFFECTS OF SPINAL ANAESTHESIA**

### **Cardiovascular effects**

Spinal anaesthesia results in a temporary sympathectomy because of this there is a drop in blood pressure from a combination of decrease in venous return that serves to decrease preload and cardiac output, and, arterial dilation causing a drop in systemic vascular resistance. There are two mechanisms by which sympathetic blockade of venous and arterial blood vessels occur; one is by direct inhibition of the nerves innervating the blood vessels, the other being a decrease in circulating catecholamines by inhibition of nerves supplying the adrenal gland.<sup>7</sup> Risk factors for development of hypotension during spinal anaesthesia

- Increasing age
- Block height higher than T5
- A baseline systolic blood pressure <120 mm of Hg
- Dural puncture at or above L2-L3 interspace
- Combined general and neuraxial anaesthesia

Heart rate is a complex function of a balance between the sympathetic and parasympathetic nervous systems. The effect of spinal anaesthesia on heart rate is inversely proportional to the spinal block height, higher the block lesser the heart rate. Maintenance of adequate preload may be the key to a decrease in the incidence of bradycardia<sup>32</sup>

## **Respiratory effects**

Spinal block height limited to lumbar and lower thoracic region have minimal clinical consequences on the respiratory system, however a block height of T5 and above may affect the ability to cough and clear secretions, this can adversely alter respiratory function in patients with respiratory disorders. There is a decrease in the oxygen demand and consumption during spinal anaesthesia probably as a result reduced metabolic demand due to decreased cardiac workload, muscle paralysis and a decrease in overall metabolism. <sup>33</sup>

## **Central nervous system effects**

Blood flow to the central nervous system remains constant because of auto regulation of cerebral blood flow except when there is profound hypotension (mean arterial pressure of < 55 mm of Hg in a normotensive individual)<sup>7</sup>

## **Coagulation system**

By influencing blood flow and altering Virchow's triad, neuraxial anaesthesia may be associated with a decreased incidence of deep vein thrombosis and pulmonary embolism as compared to general anaesthesia <sup>34</sup>

## **COMPLICATIONS OF SPINAL ANAESTHESIA**

### **Nerve injury**

Permanent or disabling nerve injury is a rare occurrence, seen as a result of direct trauma to the nerve during needle placement. Auroy et al in their survey found that two thirds of patients who developed nerve injury had parasthesia during needle placement. <sup>59</sup>

### **Post dural puncture headache (PDPH)**

PDPH is one of the commonest complications of spinal anaesthesia, with an incidence of less than 3%. It occurs due to CSF leakage from the dural defect left by the spinal needle. CSF leakage, if greater than its production, can result in low CSF pressures, this causes traction on the intracranial contents with pain referred via the trigeminal nerve to the frontal area and via the glossopharyngeal, vagus, cervical to the occiput, neck and shoulders, when the patient assumes the upright posture. PDPH generally presents in 15-48hrs and resolves in 10days in over 90% of patients. Treatment is with bed rest, adequate hydration, analgesics (NSAIDs) and caffeine.

### **Local Anaesthetic toxicity**

Though most local anaesthetics have the potential to cause neuronal damage, when used in the recommended dosage and concentrations, toxicity rarely occurs.

### **Spinal Hematoma**

Most cases developing a spinal hematoma have a coagulation defect, the remaining probably had a difficult needle placement or a bloody tap. A large hematoma if not detected and treated early can result in permanent neurological deficit. Careful patient selection and procedure can avoid this complication.

### **Central neural infections**

Arachnoiditis, meningitis, spinal abscess are rare after spinal anaesthesia. They can occur due to an exogenous source like contaminated equipment, procedure or medication, alternatively it can

be a result of endogenous source by seeding of bacteria from a remote site, making sepsis a relative contraindication for some anaesthetists.

## REVIEW OF LITERATURE

There are many factors that affect the spread, intensity and duration of spinal anaesthesia but which factor carries more importance is the question posed by many investigators. In 1987 Lambert and Covino <sup>35</sup> in their article on the understanding of density and patient positioning on success of spinal anaesthesia suggested that in procedures requiring spinal anaesthesia, if the surgery is above L1 then hyperbaric bupivacaine is more suitable but if the surgery is below L1 then isobaric bupivacaine is ideal as it can provide adequate anaesthesia without extensive dermatomal spread.

In our study 3ml of 0.25% isobaric bupivacaine was the study drug and 1.5ml 0.5% hyperbaric bupivacaine was the control drug, the total dose however kept constant at 7.5mg was based on few studies that showed dose of local anaesthetic being more important than the concentration or the volume of bupivacaine.

In 1990 LANZ et al <sup>36</sup> conducted a double blinded study on 60 patients, who were given varying concentration and volume of isobaric bupivacaine while keeping the total dose of bupivacaine same, they found no difference among the groups with regard to the speed of onset, maximal spread, regression of sensory and motor block except in the group which received 10 ml of 0.175% isobaric bupivacaine where complete regression was faster, they however concluded that the dose was more important than either volume or concentration in isobaric bupivacaine.

A similar study by Malinovsky <sup>37</sup> in 1999 compared different volumes of isobaric and hyperbaric bupivacaine, they concluded that volume did not affect the extent of cephalad spread or duration of anaesthesia, but offset of anaesthesia was shorter with hyperbaric bupivacaine compared to isobaric bupivacaine.

Thage et al <sup>24</sup> in their review of factors affecting spread of anaesthesia stated that the dose of bupivacaine was significant importance while the age, baricity and speed of injection was of modest importance. Teckelenburg-Weier et al <sup>38</sup> as well compared the effect of patient positioning (Tredelenburg) on the spread of sensory block after spinal anaesthesia using hyperbaric and isobaric bupivacaine, they concluded that the baricity did not influence the spread of the drug. As clearly stated by Hocking and Wildsmith <sup>39</sup> in their review article on intrathecal drug spread, though many factors affect the spread of a local anaesthetic, their role is minor unpredictable and at times beyond the physician's control. The major factors are the baricity of the solution and the position of the patient immediately after the spinal block.

The primary aim in our study was to evaluate whether isobaric bupivacaine provides more stable hemodynamics compared to hyperbaric bupivacaine, this hypothesis was based on many previous studies, but our study population was exclusively ASA II and ASA III patients which has not been done before and in whom acquirement of stable hemodynamics is most desirable.

Phelan et al <sup>40</sup> concluded that hyperbaric bupivacaine resulted in a more rapid fall in blood pressure but had a more predictable dermatome level compared to isobaric bupivacaine after conducting a study on 67 patients in which p value was found to be statistically significant.

Shimai et al <sup>41</sup> when conducting a study on 45 patients with differing baricity and volume but same concentration found a more severe drop in blood pressure with hyperbaric bupivacaine of comparatively larger volume, their suggestion was that adequate anesthesia with a lesser drop in blood pressure could be obtained with a larger volume but lesser baricity of bupivacaine or a lower volume and higher baricity.

In this study by Vernhiet J et al <sup>42</sup> conducted on 264 patients hyperbaric bupivacaine was found to a faster onset, higher level and longer duration of spinal block but had a greater fall in blood pressure than isobaric bupivacaine.

Rama et al <sup>43</sup> in their study done in 2002 on 60 patients comparing hyperbaric, isobaric and hypobaric bupivacaine found no difference in the hemodynamic changes, level of analgesia, degree of motor block or duration of anaesthesia amongst all three groups.

Roberts et al <sup>44</sup> in a double blind study of 90 patients observed that hyperbaric bupivacaine provides rapid and intense sensory block of intermediate duration while isobaric bupivacaine provides a longer duration of action with a lesser block height and lesser cardiovascular disturbance.

Siaens et al <sup>45</sup> compared three different solutions of bupivacaine for spinal anaesthesia. Group 1 received 10mg hyperbaric bupivacaine, group 2 got 10mg isobaric bupivacaine while group 3 received 15mg isobaric bupivacaine. In the first two groups cephalad spread, analgesia duration, motor block and the decrease in mean arterial pressure were comparable. But group 3 had a higher cephalad spread, longer duration of analgesia and more pronounced motor block, though the mean arterial pressure drop was comparable to the other groups.

Tattersall <sup>46</sup> compared isobaric bupivacaine (15mg) with hyperbaric amethocaine (10-16mg) in 123 patients undergoing various surgeries. Patients who received isobaric bupivacaine had a comparatively limited spread of analgesia that lasted longer associated with lesser hypotension.



## MATERIALS AND METHODS

A randomized double blinded study was conducted on ASA II and ASA III patients coming for lower limb surgery. Sample size estimation was done based on a similar study by Paul et al 2001 where the mean difference in the outcome (SD) was 11.69. For a level of significance of 5% and power of study of 80%, sample size was estimated to be 180 in each group.

#### Inclusion criteria

- Age more than 20 years (adult patients)
- ASA II and ASA III
- Lower limb general surgery procedures like debridement, amputation, split thickness skin grafting

#### Exclusion criteria

- Patient refusal
- Coagulation disorders
- Current treatment with antiplatelets except aspirin
- Sepsis
- Dehydration
- Spinal canal anomalies
- Height <150cm

#### Randomization

Randomization of 130 patients was done using shuffled sealed envelopes after generating the random numbers from a computer. Block randomization was done to ensure equal allocation in

each group, resulting in 65 patients in each group. The patient and outcome assessor was blinded to the drug making it a double blinded study.

Control group: received 1.5ml of 0.5% hyperbaric bupivacaine

Study group: received 3ml of isobaric 0.25% isobaric bupivacaine

For the study drug 1.5ml of 0.5% bupivacaine was diluted with 1.5ml of saline (sterile)

### Procedure

After taking informed consent, demographic criteria and a recording of preoperative systolic and diastolic blood pressure was noted. An intravenous line with an 18G or 20G cannula was established. All patients received 1mg of IV midazolam for anxiolysis. Preloading with 500ml of crystalloid solution was done for all patients to reduce possible hypotension, further fluids were given at a maintenance rate of 2ml/kg apart from replacement of blood loss. All patients received 6l/min of O<sub>2</sub> via a face mask.

Standard monitoring was done in both groups utilizing electrocardiography, non invasive blood pressure measurement and pulse oximetry.

### Assessment and management

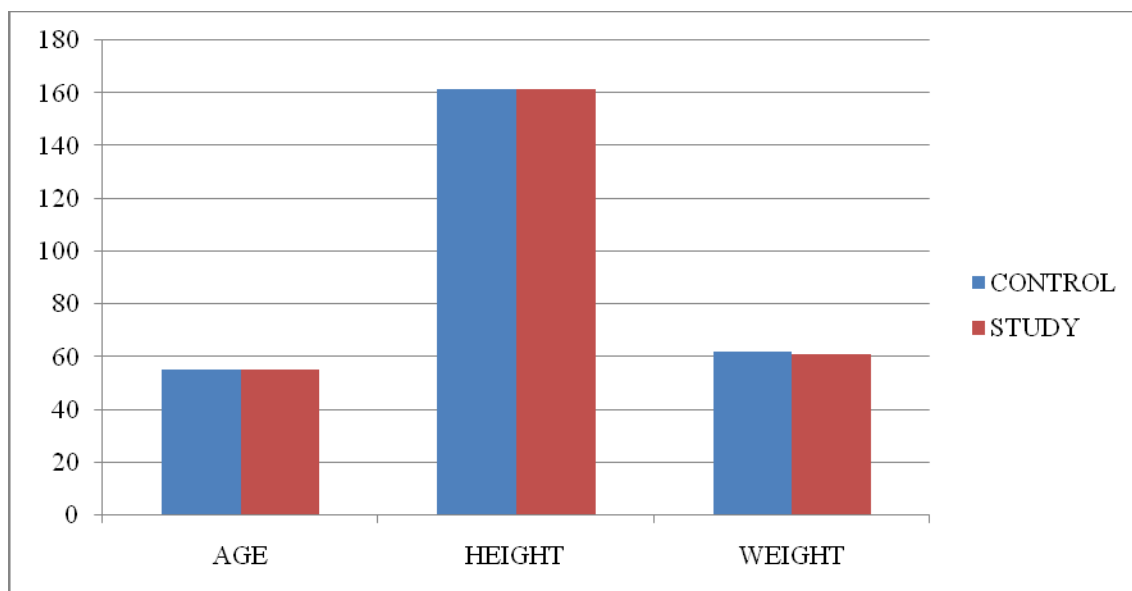
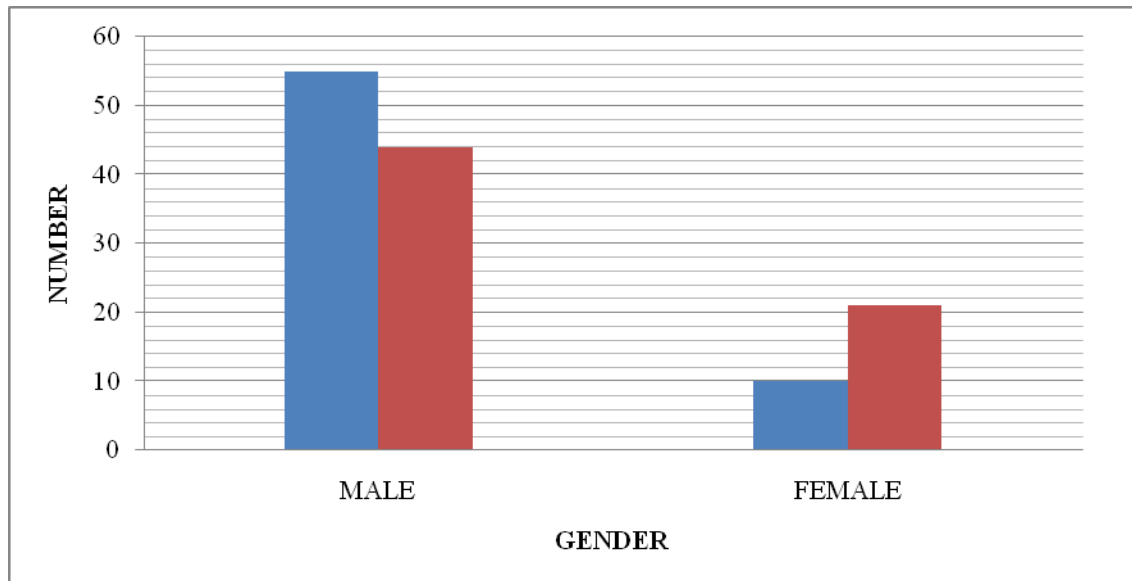
After taking a baseline recording of heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure and oxygen saturation, recording were noted every 3mins for the first 15mins, then every 5 mins for half an hour, every 10mins for one hour and then every 15mins thereafter. A drop in systolic blood pressure to less than 100 mm of Hg or 20% from baseline, or a drop in mean arterial pressure of less than 65mm of Hg or 20% from baseline was treated with intravenous boluses of either 50 – 100 mcg of phenylephrine or 5mg of ephedrine.

A heart rate of less than 50bpm was treated with IV atropine 0.6mg. A drop in saturation or respiratory difficulty if any was treated with assisted ventilation using 100% O<sub>2</sub>. Sensory block assessment was done using pin prick while motor block was assessed using the modified Bromage scale. Time for onset was taken from the time of giving intrathecal drug to onset of block. Duration of sensory block was taken from the time of onset to complete regression of the block. Incomplete or patchy block was given general anaesthesia or the procedure was repeated, supplemental analgesia was provided whenever needed with boluses of intravenous fentanyl or morphine, till pain free.

### Technique

Patient was positioned in the lateral position with the affected limb in the dependant position. The back, hips and knees were flexed by an assistant to facilitate needle placement. Subarachnoid block was performed with 25G Whitacre needle at L3-4 or L4-5 interspace, on clear tap of CSF, the drug was injected after reconfirmation of CSF aspiration. Patient was then placed supine and assessment done.

## RESULTS

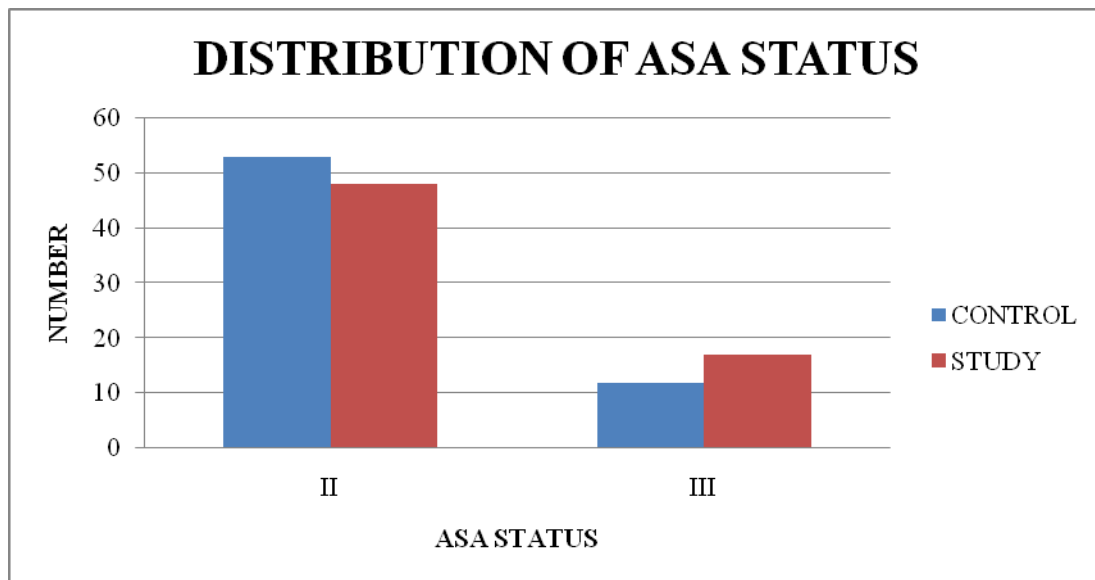


### **DEMOGRAPHIC DATA**

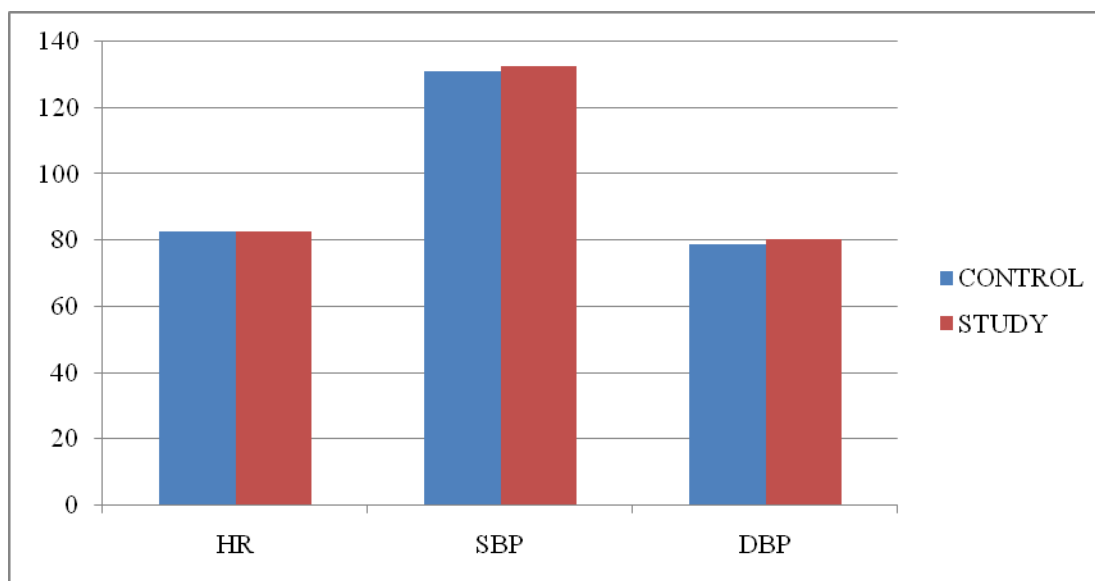
	<b>MALE</b>	<b>FEMALE</b>
<b>CONTROL</b> (in no.)	<b>55</b>	<b>10</b>
<b>STUDY</b> (in no.)	<b>44</b>	<b>21</b>

<b>Mean <math>\pm</math> S.D</b>	<b>AGE</b>	<b>HEIGHT</b>	<b>WEIGHT</b>
<b>CONTROL</b>	55.11 $\pm$ 10.11	161.66 $\pm$ 13.5	61.91 $\pm$ 9.13
<b>STUDY</b>	55.28 $\pm$ 10.8	161.6 $\pm$ 7.25	61.22 $\pm$ 10.86

There was no significant difference between the two groups with regard to age, gender, height and weight



### PRE-OPERATIVE VITALS





### **PATIENT VARIABLES**

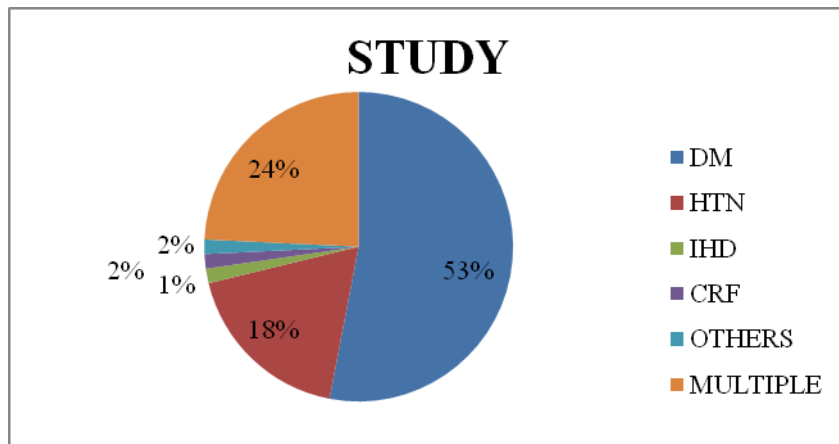
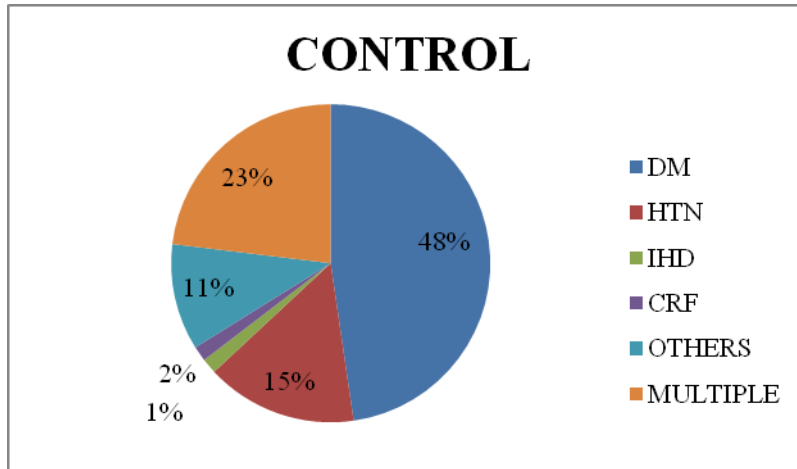
	<b>ASA II</b>	<b>ASA III</b>
<b>CONTROL</b> (in no.)	<b>53</b>	<b>12</b>
<b>STUDY</b> ( in no.)	<b>48</b>	<b>17</b>

### **PRE OP VITALS**

<b>Mean <math>\pm</math> S.D</b>	<b>Heart rate</b>	<b>Systolic blood pressure</b>	<b>Diastolic blood pressure</b>
<b>CONTROL</b>	82.57 $\pm$ 13.73	131.08 $\pm$ 17.47	78.8 $\pm$ 11.95
<b>STUDY</b>	82.77 $\pm$ 13.15	132.48 $\pm$ 17.18	80.25 $\pm$ 10.85

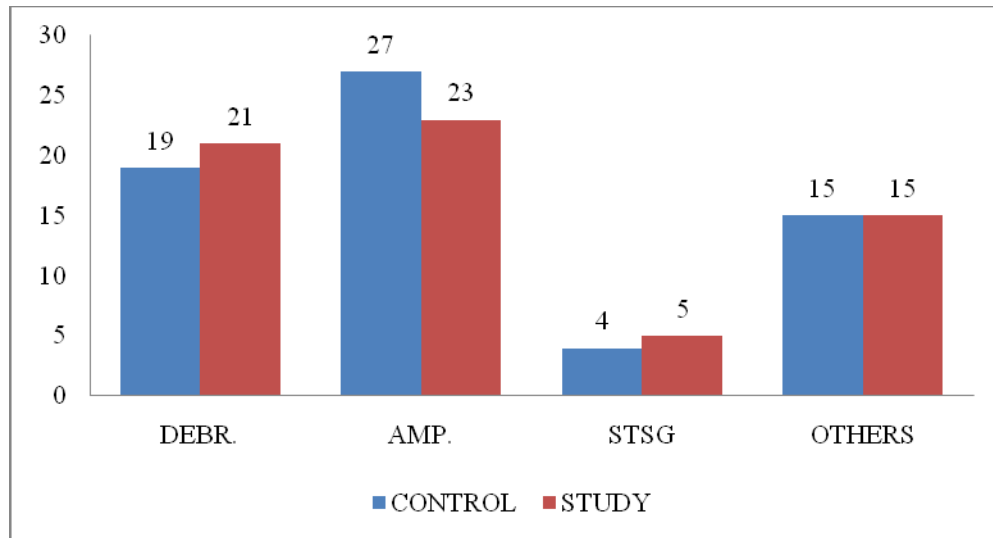
The distribution of ASA II and ASA III patients in both the groups were comparable, there was not much difference between preoperative vitals in both the groups.

## DISTRIBUTION OF SYSTEMIC ILLNESSES BETWEEN THE TWO GROUPS



**DISTRIBUTION OF SYSTEMIC ILLNESSES BETWEEN THE TWO GROUPS**

	<b>DM</b>	<b>HTN</b>	<b>IHD</b>	<b>CRF</b>	<b>OTHERS</b>	<b>MULTIPLE</b>
<b>CONTROL</b> ( in no.)	<b>31</b>	<b>10</b>	<b>1</b>	<b>1</b>	<b>7</b>	<b>15</b>
<b>STUDY</b> ( in no.)	<b>35</b>	<b>12</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>16</b>

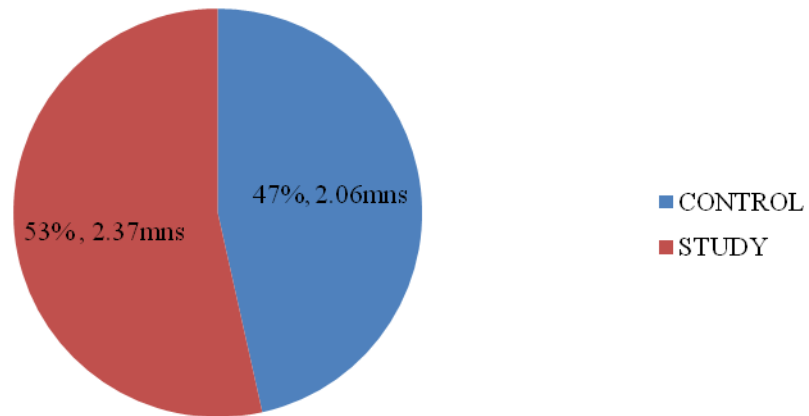


**DISTRIBUTION OF SURGERIES BETWEEN THE TWO GROUPS**

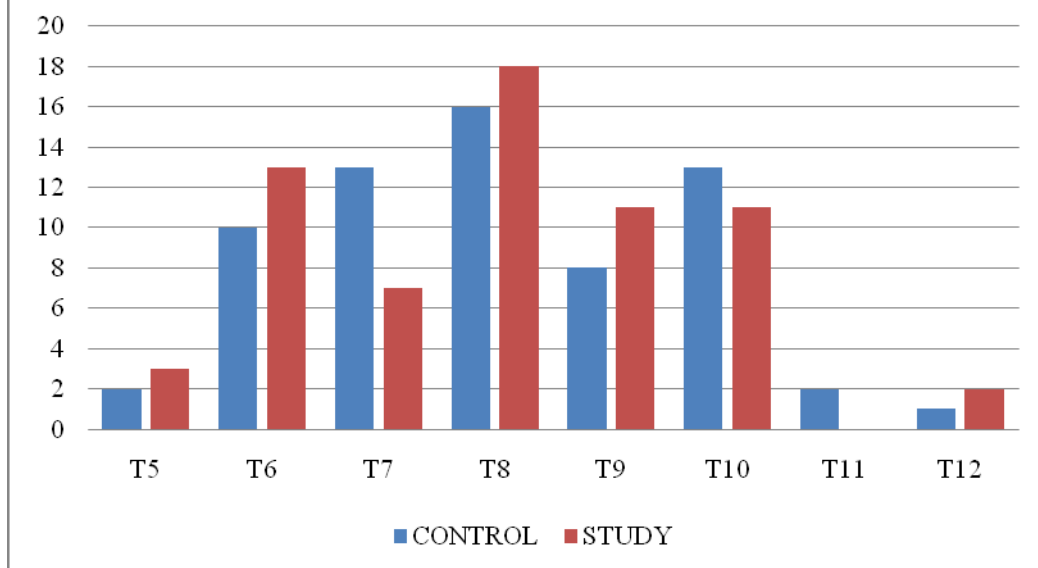
	<b>DEBR.</b>	<b>AMP.</b>	<b>STSG</b>	<b>OTHERS</b>
<b>CONTROL ( in no.)</b>	<b>19</b>	<b>27</b>	<b>4</b>	<b>15</b>
<b>STUDY ( in no.)</b>	<b>21</b>	<b>23</b>	<b>5</b>	<b>15</b>

The distribution of the systemic illnesses and type of surgery was similar in both groups.

## PERCENTAGE DISTRIBUTION OF AVERAGE TIME FOR ONSET



## AVERAGE BLOCK HEIGHT



#### TIME FOR ONSET OF MAXIMAL CEPHALAD BLOCK

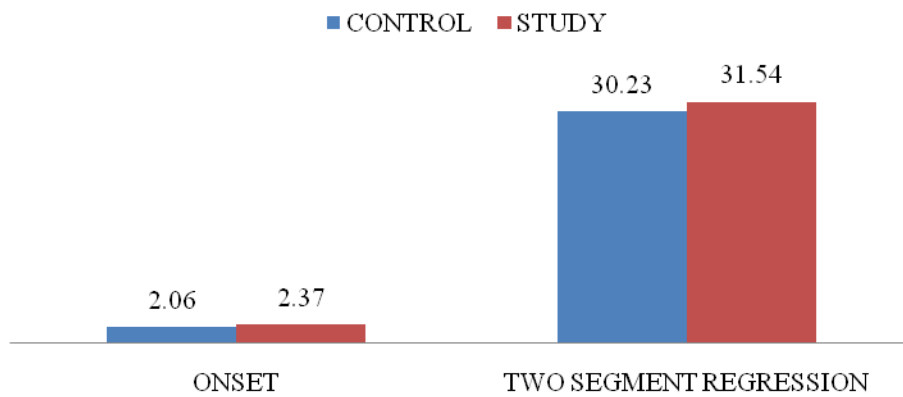
	Average onset in mins	Percentage distribution	Std.deviation	p value
CONTROL	2.06	47%	1.014	0.12
STUDY	2.37	53%	1.219	

#### AVERAGE DERMATOMAL SPREAD OF SENSORY ANAESTHESIA

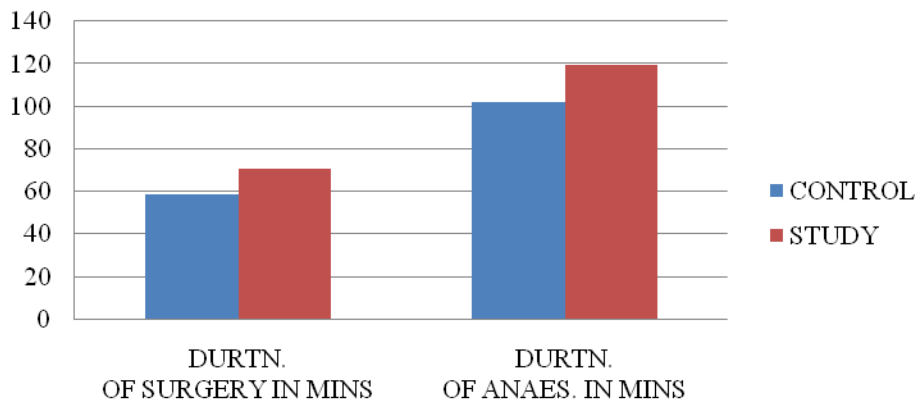
	CONTROL	STUDY
T5	2	3
T6	10	13
T7	13	7
T8	16	18
T9	8	11
T10	13	11
T11	2	0
T12	1	2

The average spread of maximal sensory block was T8 in both groups, which is higher than required, while the mean onset of spinal anaesthesia was about 2mins in both groups.

### Time for onset of block and time to two segment regression



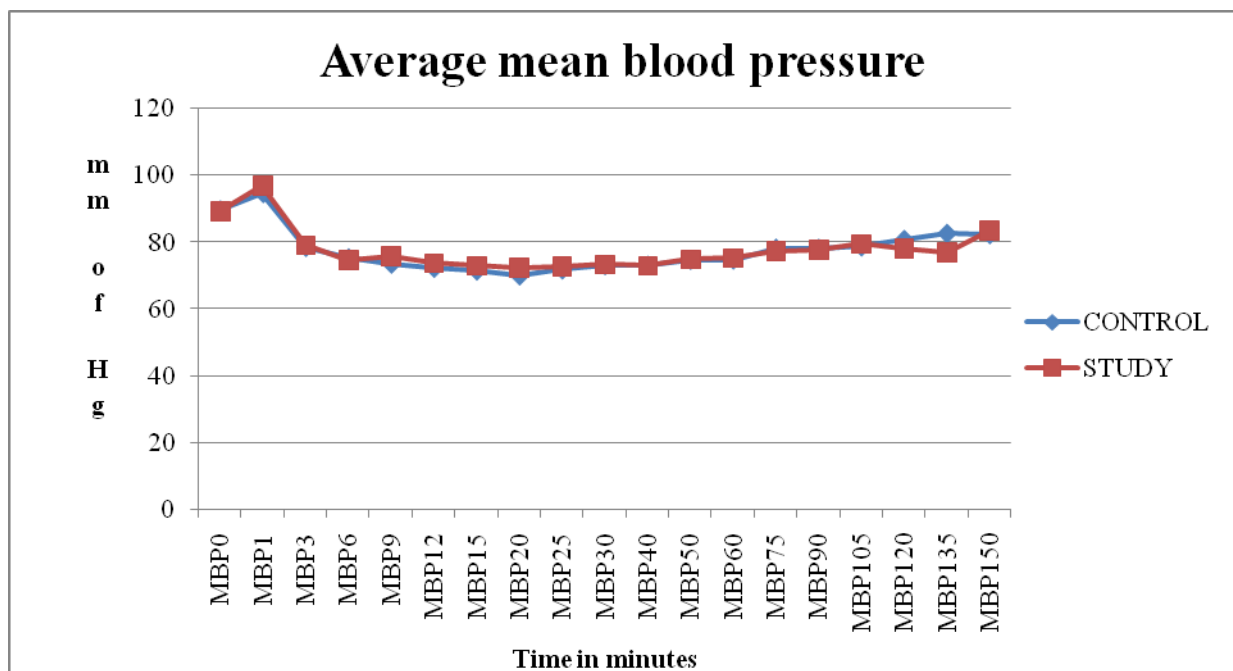
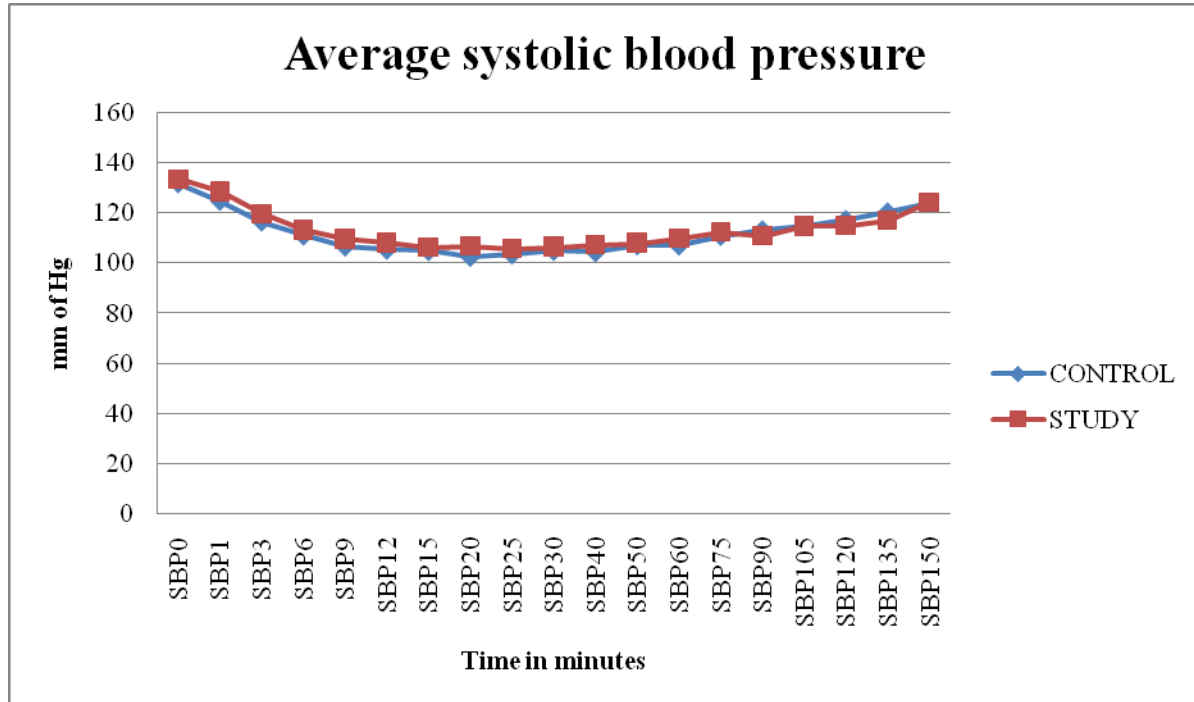
### Duration of procedure and Anaesthesia





Values in mins. $\pm$ S.D	CONTROL	STUDY	p value
Time to block onset	2.06 $\pm$ 1.014	2.37 $\pm$ 1.219	0.12
Two segment regression	30.23 $\pm$ 8.265	31.54 $\pm$ 7.011	0.33
Duration of surgery	58.38 $\pm$ 26.05	70.62 $\pm$ 30.61	.015
Duration of anaesthesia	101.85 $\pm$ 24.07	119.54 $\pm$ 26.51	0.00*

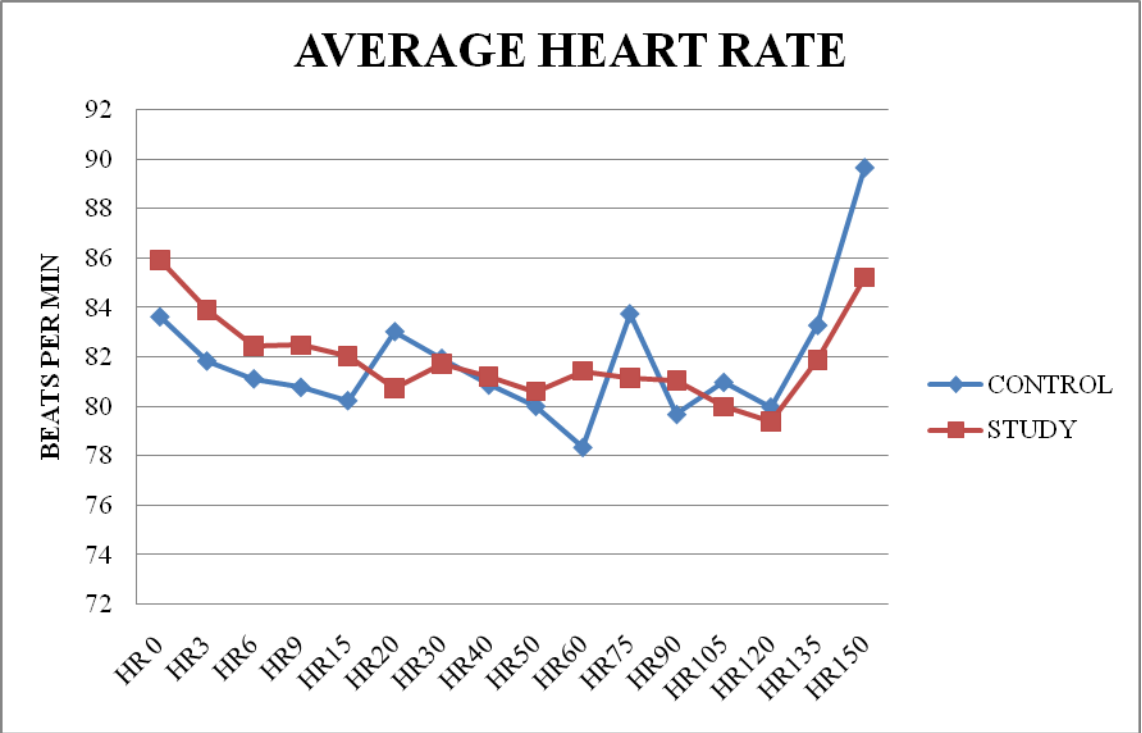
The time for onset of maximal cephalad block and two segment regression did not differ between the two groups, but duration of anaesthesia was significantly longer in the study group with a p value of 0.000.



### AVERAGE BLOOD PRESSURE (SYSTOLIC AND MEAN) IN BOTH GROUPS

Time in mins	Control	Study	p value		Control	Study
	SBP	SBP			MBP	MBP
0	131.89 $\pm$ 17.38	133.54 $\pm$ 17.66	0.59	0.95	89.5 $\pm$ 11.74	89.43 $\pm$ 10.8
3	116.54 $\pm$ 19.05	119.77 $\pm$ 18.72	0.32	0.79	78.58 $\pm$ 12.19	79.18 $\pm$ 14.24
9	106.59 $\pm$ 15.44	109.05 $\pm$ 21.45	0.45	0.19	73.60 $\pm$ 10.3	76.05 $\pm$ 10.78
15	104.74 $\pm$ 12.11	106.15 $\pm$ 18.24	0.60	0.39	71.58 $\pm$ 10.25	73.12 $\pm$ 10.21
20	102.40 $\pm$ 12.46	106.80 $\pm$ 15.6	0.67	0.18	76.11 $\pm$ 10.38	72.46 $\pm$ 9.76
30	104.77 $\pm$ 11.31	106.52 $\pm$ 11.66	0.38	0.82	73.18 $\pm$ 8.52	73.51 $\pm$ 8.07
40	104.25 $\pm$ 10.38	107.17 $\pm$ 12.49	0.14	0.98	73.15 $\pm$ 8.34	73.12 $\pm$ 11.6
50	107.03 $\pm$ 10.26	108.00 $\pm$ 11.37	0.61	0.86	74.75 $\pm$ 8.46	75.03 $\pm$ 9.33
60	10.94 $\pm$ 9.36	109.92 $\pm$ 11.16	0.16	0.73	74.82 $\pm$ 8.18	75.42 $\pm$ 11.64
75	110.80 $\pm$ 8.94	112.38 $\pm$ 12.6	0.42	0.61	78.23 $\pm$ 7.99	77.45 $\pm$ 9.05
90	113.3 $\pm$ 9.19	110.85 $\pm$ 14.11	0.28	0.84	78.17 $\pm$ 7.33	77.85 $\pm$ 9.08
105	114.59 $\pm$ 10.12	114.68 $\pm$ 10.36	0.96	0.61	78.70 $\pm$ 6.93	79.56 $\pm$ 9.31
120	117.41 $\pm$ 12.88	115.07 $\pm$ 9.80	0.37	0.20	80.79 $\pm$ 8.28	78.35 $\pm$ 7.77
135	120.46 $\pm$ 14.15	117.10 $\pm$ 10.74	0.39	0.24	82.2 $\pm$ 8.73	77.10 $\pm$ 15.59
150	124.17 $\pm$ 15.56	124.46 $\pm$ 12.7	0.96	0.74	82.33 $\pm$ 7.65	83.69 $\pm$ 8.47

There was no statistically significant difference in the average systolic and mean blood pressure between the two groups.



### AVERAGE HEART RATE IN BOTH THE GROUPS

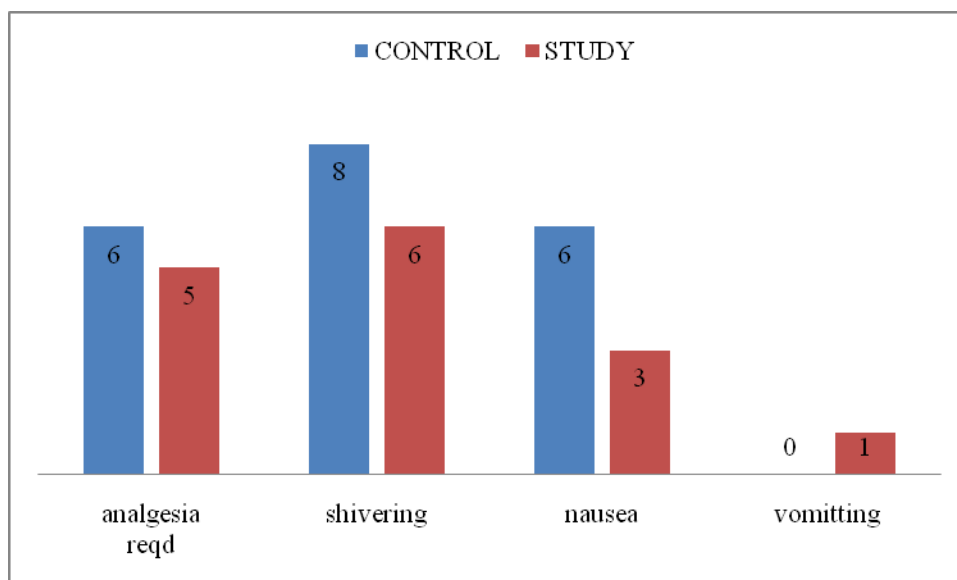
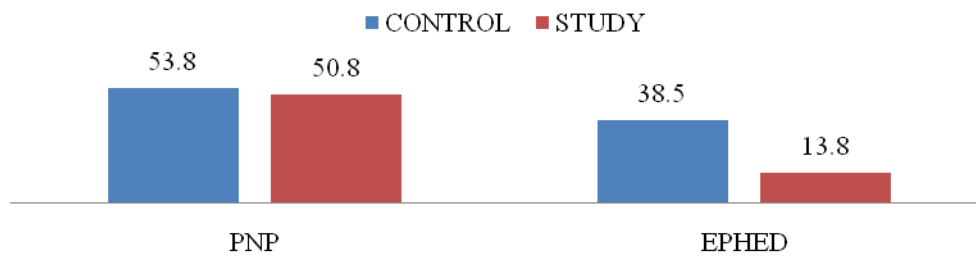
TIME IN MINS	CONTROL GROUP HEART RATE	STUDY GROUP HEART RATE	p VALUE
0	83.65 $\pm$ 13.75	85.95 $\pm$ 13.45	0.33
3	81.86 $\pm$ 13.74	83.92 $\pm$ 12.69	0.37
9	80.8 $\pm$ 12.90	82.5 $\pm$ 113.74	0.45
15	80.26 $\pm$ 15.7	82.05 $\pm$ 12.9	0.48
20	83.05 $\pm$ 12.08	80.75 $\pm$ 16.51	0.36
30	81.97 $\pm$ 12.89	81.75 $\pm$ 12.9	0.925
40	80.89 $\pm$ 12.39	81.23 $\pm$ 12.68	0.878
50	80.03 $\pm$ 12.34	80.62 $\pm$ 15.56	0.813
60	78.37 $\pm$ 13.47	81.45 $\pm$ 11.81	0.169
75	83.77 $\pm$ 28.34	81.16 $\pm$ 11.66	0.498
90	79.7 $\pm$ 10.5	81.08 $\pm$ 11.95	0.515
105	81 $\pm$ 11.23	80.35 $\pm$ 11.11	0.773
120	80 $\pm$ 12.95	79.4 $\pm$ 16.7	0.875
135	83.3 $\pm$ 13.59	81.9 $\pm$ 12.2	0.732
150	89.67 $\pm$ 13.5	85.23 $\pm$ 15.40	0.553

There was no statistical difference in the heart rate between the two groups.

## TOTAL VASSOPRESSOR REQUIRMENT



## PERCENTAGE REQUIRING VASSOPRESSORS



	<b>CONTROL</b>	<b>STUDY</b>	<b>p value</b>
<b>PHENYLEPHRINE (in no.)</b>	<b>35</b>	<b>33</b>	<b>1.00</b>
<b>EPHEDRINE (in no.)</b>	<b>25</b>	<b>9</b>	<b>0.17*</b>

<b>IN no. and %</b>	<b>CONTROL</b>	<b>STUDY</b>	<b>pVALUE</b>
<b>ANALGESIA REQD.</b>	<b>6 (9.2%)</b>	<b>5 (7.7%)</b>	<b>0.754</b>
<b>SHIVERING</b>	<b>8 (12.3%)</b>	<b>6 (9.2%)</b>	<b>0.57</b>
<b>NAUSEA</b>	<b>6 (9.2%)</b>	<b>3 (4.6%)</b>	<b>0.303</b>
<b>VOMITTING</b>	<b>0</b>	<b>1 (1.5%)</b>	<b>0.319</b>

The requirement for ephedrine was significantly less in the study group with a p value of <0.05.

The supplemental analgesic requirement did not differ much between the two groups, the incidence of shivering, nausea, vomiting was similar in both groups.

## DISCUSSION



The incidence of systemic illnesses like diabetes mellitus, hypertension is on the rise probably because of early detection or lifestyle changes, whatever the reason, the anaesthetists role is to preserve organ function when these patients come for surgery. This is easier said than done.

An eternal debate is whether general or regional anaesthesia is better for these subset of patients, arguably most studies have not shown a clear margin of benefit between general and regional anaesthesia. Regional anaesthesia however is said to have certain beneficial effects. In an overview of randomized trials comparing effects of general and neuraxial anaesthesia on postoperative morbidity and mortality by Rogers A et al <sup>47</sup>, neuraxial blockade reduced the odds of deep vein thrombosis by 44%, pulmonary embolism by 55%, transfusion requirements by 50%, pneumonia by 39%, and respiratory depression by 59% (all  $P < 0.001$ ). There were also reductions in myocardial infarction and renal failure. Post operative cognitive dysfunction is common in the elderly and can be associated with increased risk for postoperative morbidity and mortality, general anaesthesia was found to be associated with increased risk for early (3 days) post operative cognitive dysfunction <sup>48</sup> although incidence of long term post operative cognitive dysfunction did not differ in patients receiving either general or regional anaesthesia. <sup>49</sup>

Non healing foot ulcer and gangrene were the commonest diagnosis for which surgery was undertaken. Surgery for the for these conditions, is a relatively minor operation with negligible blood loss, but providing anesthesia for these patients is a frequent challenge because of serious comorbidities.

Cardiovascular autonomic neuropathy is associated with increased morbidity and mortality <sup>50</sup>, and hemodynamic instability is common in patients with autonomic dysfunction during anesthesia induction and maintenance <sup>51,52</sup>. It is important to maintain anesthesia as stable as

possible including adequate analgesia. Although there is no clear evidence that one type of anesthetic is superior for patients with coexisting medical illnesses, the stress response to surgery may be reduced with combinations of local or regional anesthesia and the administration of opioids <sup>53</sup>.

Regional anesthesia is a reasonable choice for lower extremity operations in most patients mainly diabetics <sup>54</sup>. When spinal anesthesia is planned, high sensory block levels are not required, especially when a tourniquet is not used. Limiting the block to lower dermatomal levels and avoiding the occurrence of hypotension is important because fluid loading and vasopressor administration may not be ideal methods to prevent or treat hypotension since end-stage renal disease and coronary artery occlusive disease are common in these patients. It has been suggested that when compared with the general population, patients with preexisting sensorimotor neuropathy or diabetic polyneuropathy may be at increased risk of further neurologic sequelae after neuraxial anesthesia or analgesia <sup>55,56</sup>. Diabetic nerve fibers may be more susceptible to the toxic effects of local anesthetics <sup>56</sup>. Minimizing the concentration of local anesthetics can be safe for patients undergoing diabetic foot surgery.

In our study, the primary aim was to find out which concentration and baricity of local anaesthetic provided better hemodynamic stability, the hypotension with isobaric spinal anaesthesia was marginally lesser than that seen in the control group, though the p value was not significant.

This is in keeping with the finding of Malinovsky et al <sup>23</sup> who studied 90 patients to determine the effects of volume and baricity of bupivacaine on hemodynamics, they also found no difference in the block onset and maximum cephalad spread, although the offset of anaesthesia was longer with isobaric bupivacaine which is similar to the findings in our study, where the mean duration

of anaesthesia was longer in isobaric group with a p value of  $<0.05$ . Solakovic<sup>57</sup>, however found a greater drop in blood pressure and heart rate in patients receiving hyperbaric bupivacaine as compared to isobaric bupivacaine.

Hypotension, defined by a drop in systolic blood pressure by more than 20% from baseline, was treated with vasopressors, phenylephrine was given in doses of 50 mcg in most cases, and ephedrine in boluses of 5 mg was used when the heart rate was lower than 70bpm. The consumption of phenylephrine was no different between the two groups but that of ephedrine was significantly lesser with a p value of 0.017 in the isobaric bupivacaine probably serving as indirect indicator of increased slowing of heart rate in the hyperbaric bupivacaine, although actual comparison of heart rate at various time points did not show any significant difference between the two groups. Our study showed that both groups had stable hemodynamics, hence 0.25% isobaric bupivacaine can safely be used in patients with decreased cardiac reserve.

The time for onset of maximal cephalad block was similar in both the groups. Both groups had equally effective sensory and motor blockade. The distribution of block height was similar in both groups with an average block height of around T8, this is more than necessary for lower limb surgery and probably contributed to the hypotension<sup>58</sup>. The incidence of side effects like nausea, vomiting, shivering, urinary retention, post dural puncture headache was not different between the two groups. Requirement for additional analgesia was similar between the two groups. In effect isobaric bupivacaine renders spinal anaesthesia similar to hyperbaric bupivacaine albeit with a longer duration, which can be utilized as an advantage. The limitation in this study is the need for a larger sample size.

## CONCLUSION

## **CONCLUSION**

The spread of local anaesthetic is dependent upon the mass of local anaesthetic and not on its concentration as evidenced by similar time for onset, height of block and intensity of sensory and motor block, which was adequate in both the groups; however the duration of block was significantly longer in the isobaric group. 0.25% isobaric bupivacaine is as effective as 0.5% bupivacaine in providing stable hemodynamics and hence can safely be used in patients with decreased cardiac reserve.

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## APPENDIX

### **PROFORMA FOR 0.25%/ 0.5% BUPIVACAINE STUDY FOR SPINAL ANAESTHESIA**

NAME:

SERIAL NO.:

AGE:

DATE:

SEX:

SURGERY UNIT:

WEIGHT:

WARD:

ASA GRADE: II/III

GROUP: 1      2    {1= 1.5ml of 0.5% spinal bupivacaine

2= 3ml of 0.25% spinal bupivacaine}

Diagnosis:

Co-morbid illness with duration:

Pre-op: PR-

BP-

Time of giving spinal:

Time of onset of block:

Level of spinal block:

Intra-op: nausea – Y/N    vomiting – Y/N

Analgesia: adequate/ inadequate

Post- op: duration of analgesia:

Nausea-Y/N      Vomiting – Y/N

Mins	Dermatome	Bromage Scale	SBP	DBP	MBP	PR	SpO2	Drugs E5/P50
0								
1								
3								
6								
9								
12								
15								
20								
25								
30								
40								
50								
60								
75								
90								
105								
120								
135								
150								
165								
180								

Adverse effects: Y/N (plz mention which adverse effect occurred)

Inclusion: all ASA II and above, adult surgery patients for lower limb surgery, in whom spinal anaesthesia is planned

Exclusion: ASA I, any contraindication for spinal, possible sepsis

Study drug: take 1.5ml of (heavy) 0.5% Bupivacaine and add 1.5ml of sterile saline, and give entire 3ml.

Control drug: 1.5ml of (heavy) 0.5% Bupivacaine



## **ABSTRACT**

**Name of guide: Dr. Sarah Ninan, Professor and HOD, Department of Anaesthesia, CMCH, Vellore**

**Name of Course: M.D Anaesthesiology**

### **Aims and Objectives:**

To compare the efficacy of two solutions of bupivacaine, 1.5ml of 0.5% bupivacaine and 3 ml of 0.25% hyperbaric bupivacaine in providing stable hemodynamics.

To compare the time of onset, height of block, intensity of sensory and motor blockade, duration of analgesia as well as the incidence of side effects between the two groups.

### **Materials and methods:**

After sample size estimation based on a similar previous study by Paul et al 130 ASA II and ASA III patients were randomized by a computer generated sequence into two equal groups of 65 patients each, the control group received 1.5ml of 0.5% bupivacaine while the study group received 3 ml of 0.25% hyperbaric bupivacaine.

Patient and outcome assessor were blinded making it a double blinded study.

### **Results:**

Both the groups provided good hemodynamic stability.

Onset and intensity of sensory and motor blockade was equally good in both groups with a p value of 0.12 and 0.33 respectively. The maximal cephalad spread of local anaesthetics was also similar in both groups.

The occurrence of side effects such as nausea, vomiting and urinary retention did not differ between the two groups.

However the duration of analgesia (p value 0.00) and requirement of vassopressors (control 59% and study 41%) was significantly less in the isobaric (0.25%) group.

**Conclusion:**

0.25% isobaric bupivacaine is as effective as 0.5% hyperbaric bupivacaine in providing stable hemodynamics in patients with decreased cardiac reserve.

## **KEY TO MASTER CHART**

S.No. – serial number

Hosp. No. – hospital number

Gend. – Gender: male-1

Female-2

Ht/ Wt – height / weight

Grp. – group 1 – control

Group 2 – study

Diag. – diagnosis -

Diabetes-1

Hypertension – 2

Ischaemic heart disease – 3

Chronic renal failure – 4

Others – 5

Type of surgery:       debridement- 1

Amputation- 2

STSG- 3

Others – 4

HR- heart rate, SBP- systolic blood pressure, DBP- diastolic blood pressure, MBP- mean blood pressure

Pre –pre operative

Brmge scale – bromage scale

Durtn of surg – duration of surgery in minutes

Sbp0 – systolic blood pressure at 0 minutes in mm of Hg then 1minute and so forth

Dbp – diastolic blood pressure, Mbp- mean blood pressure , HR – heart rate

2 seg reg– 2 segment regression -time for anaesthesia level to decrease by segments. [ex.- from T6 to T8]

Durtn of analg- Duration of analgesia - how long the spinal anaesthesia lasts in minutes

Vassppressor- drug used to increase the blood pressure- number of times required throughout the surgery. PNP- phenylephrine, eph- ephedrine

Analg reqd- analgesia required: required – 1  
Not required – 2

Shivering, nausea, vomiting, other side effects: present – 1  
Not present - 2

S.No	Hosp. No.	age in yrs	Gend	Ht	Wt	asa grade	Grp	Diag	type of surg	pre hr	presbp	predbp	onset of block mins	dermato me level	Brmge scale	durtm of surg in mins	sbp0	dbp0	mbp0	hr0	sbp1	dbp1	mbp1	hr1	sbp3	dbp3	mbp3	hr3	sbp6	dbp6	mbp6	hr6	sbp9	dbp9	mbp9	hr9	sbp12	dbp12	mbp12	hr12	sbp15	dbp15	mbp15	hr15	sbp20	dbp20	mbp20	hr20	sbp25	dbp25	
1	640693d	49	2	155	65	2	2	1	3	86	140	80	1	T9	3	100	144	86	98	83	139	8	98	82	120	70	81	84	121	74	85	89	114	78	87	85	116	70	81	80	124	70	83	92	105	68	76	84	112	75	
3	702042c	49	1	160	67	2	2	1	1	83	130	70	1	T6	3	60	133	82	93	83	130	68	89	85	122	64	78	86	116	76	86	87	10	63	74	87	102	60	70	89	106	64	74	90	107	58	69	91	106	59	
4	704371d	61	2	152	50	2	2	1	1	120	110	80	3	T6	3	30	110	63	74	128	102	60	70	129	106	64	74	110	104	57	69	116	101	58	67	115	103	71	71	114	96	54	63	113	99	49	62	111	96	61	
9	704372d	64	2	150	50	2	2	1	1	100	100	70	2	T6	3	30	104	57	69	112	91	58	66	114	96	54	63	101	99	62	70	88	78	50	56	93	89	55	63	82	97	56	66	89	99	64	72	93	92	57	
10	475194d	53	1	159	95	2	2	2	4	68	130	80	5	T7	3	100	134	66	84	66	124	79	90	65	121	72	83	69	105	57	68	68	107	64	75	70	110	61	73	71	90	60	72	69	92	61	71	68	102	62	
11	687991d	68	1	172	65	2	2	1,3	4	84	120	60	2	T6	3	80	129	81	92	88	124	72	85	87	114	67	77	83	94	62	70	81	99	62	70	80	102	60	70	82	106	64	74	83	107	58	69	90	96	54	
14	684002d	42	1	166	65	3	2	1,2,5	4	70	110	90	3	T7	3	90	115	67	78	72	120	70	81	70	88	52	61	71	74	45	51	71	69	44	50	73	86	49	58	73	88	46	56	68	88	54	62	62	104	60	
15	620115c	65	1	170	65	2	2	1	1	78	110	70	1	T8	3	60	121	68	87	88	118	67	85	86	121	70	88	86	121	70	87	82	102	62	77	82	91	59	73	86	96	61	75	84	87	59	71	90	90	60	
16	514234D	56	1	161	55	3	2	2	2	88	160	90	2	T9	3	30	175	78	101	83	168	78	100	89	158	77	97	87	152	72	93	87	146	76	94	86	144	71	88	85	130	71	85	84	130	68	83	87	134	66	
18	489279D	51	2	165	85	3	2	1,2	4	68	140	90	1	T6	3	45	144	86	98	80	139	85	98	90	115	67	78	88	120	70	81	80	114	78	87	82	111	70	80	79	115	68	78	76	113	71	81	84	107	68	
22	187676c	72	2	170	65	2	2	1,3	2	85	140	80	1	T8	3	30	175	78	101	80	168	78	100	80	158	77	97	84	152	72	93	81	146	76	94	70	144	71	85	72	130	68	83	68	134	66	84	68	135	72	
24	411111C	53	1	168	60	2	2	2	2	68	140	90	1	T6	3	60	144	86	98	72	139	85	98	62	120	70	81	60	93	56	6	54	86	49	58	58	87	58	66	62	82	56	62	63	92	62	69	52	90	64	
25	464576d	82	2	145	40	2	2	2	1	84	131	56	5	T12	3	120	131	56	81	84	123	35	64	82	120	47	71	79	113	43	66	85	122	57	78	96	111	43	65	91	110	40	63	95	118	52	74	91	118	45	
29	608064d	48	2	155	53	2	2	1,2	2	96	120	80	1	T6	3	150	163	84	107	115	152	77	100	117	124	86	66	118	135	78	83	117	129	68	83	115	138	75	88	111	146	77	94	104	129	65	85	100	130	65	
36	762265D	72	1	160	60	2	2	1	2	88	134	74	3	T8	3	100	133	74	89	88	132	74	88	85	142	76	92	86	123	81	91	88	122	63	78	86	118	65	78	81	123	65	79	77	114	68	78	77	107	62	
37	719144D	45	2	168	60	3	2	1	1	103	120	70	4	T10	3	90	124	72	84	104	129	80	81	105	121	77	87	103	121	72	83	102	119	71	82	100	110	61	73	98	109	64	75	99	105	57	68	98	107	64	
41	191471D	47	1	175	60	2	2	1	1	64	145	96	3	T9	3	50	148	91	106	80	120	86	95	82	118	85	93	84	113	64	74	82	101	50	62	82	115	60	72	76	120	70	80	89	99	62	70	84	96	54	
42	649060C	29	2	155	60	3	2	5	3	72	130	90	4	T10	3	30	135	72	87	76	124	72	84	77	129	80	81	75	121	77	87	76	124	79	89	73	121	72	83	77	120	71	82	70	116	67	79	73	115	67	
44	712554D	76	1	170	75	2	2	1	1	72	160	90	4	T10	3	50	150	80	96	100	130	71	85	93	130	68	83	82	134	66	84	82	128	80	81	85	121	68	81	87	121	74	85	80	116	70	80	81	115	78	
46	715035D	69	1	150	70	3	2	1	1	84	165	76	3	T10	3	90	148	91	106	80	142	75	91	82	128	76	88	83	129	75	89	84	126	71	85	85	124	73	84	85	116	76	86	81	115	70	80	83	115	60	
47	006204B	69	1	155	55	3	2	1	2	82	140	80	5	T9	3	100	145	70	88	86	140	72	86	83	130	71	85	80	134	66	84	81	125	86	91	86	126	70	82	83	123	75	85	84	110	60	72	85	112	70	
48	578923D	32	1	165	85	2	2	4	4	68	140	90	3	T5	3	60	133	89	99	72	133	82	93	70	113	64	74	73	101	50	64	75	95	61	69	59	91	66	68	60	93	56	65	64	98	53	68	71	91	62	
52	9184115C	53	1	155	65	2	2	1	3	68	130	70	1	T8	3	75	127	68	84	70	127	61	73	62	95	69	75	60	86	57	61	58	90	64	70	52	95	61	68	77	97	63	70	81	93	60	66	76	104	68	
53	640693D	49	2	165	50	2	2	1,2	4	92	120	70	2	T6	3	120	111	61	74	88	111	67	78	85	103	49	60	82	95	52	60	86	92	62	69	87	103	55	65	83	84	45	55	88	92	48	58	73	90	50	
54	921044	39	2	160	60	2	2	2	4	82	150	90	3	T7	3	90	151	82	97	81	141	84	97	80	109	64	7	87	10	57	68	73	107	64	75	68	114	66	78	78	114	67	79	75	116	67	79	83	109	58	
61	675629A	54	1	155	56	2	2	2	4	64	120	90	1	T7	3	90	116	60	74	98	112	64	76	66	106	65	74	67	83	48	56	68	94	66	71	69	97	55	65	67	91	58	66	63	105	57	68	60	116	60	
63	652850D	41	2	155	60	2	2	1	4	78	110	80	1	T6	3	30	137	70	87	78	130	68	84	77	122	64	78	76	91	45	57	73	105	68	77	72	112	56	71	70	100	51	63	80	114	58	73	83	110	63	
66	642990D	63	1	178	81	2	2	2	4	62	150	80	2	T10	3	60	121	94	85	62	116	70	80	63	105	68	76	65	96	62	70	68	113	71	81	71	111	70	80	74	135	79	92	72	88	46	56	79	124	72	
67	298213C	62	1	156	64	2	2	1,4	4	86	150	90	1	T5	3	75	169	97	115	86	165	105	119	84	126	80	91	82	123	75	86	79	87	58	66	88	82	56	62	91	83	59	65	89	95	69	75	85	99	73	
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77	620545	62	1	165	65	2	2	2	1	95	160	80	3	T10	3	120	148																																		

mbp25	hr25	sbp30	dbp30	mbp30	hr30	sbp40	dbp40	mbp40	hr40	sbp50	dbp50	mbp50	hr50	sbp60	dbp60	mbp60	hr60	sbp75	dbp75	mbp75	hr75	sbp90	dbp90	mbp90	hr90	sbp105	dbp105	mbp105	hr105	sbp120	dbp120	mbp120	hr120	sbp135	dbp135	mbp135	hr135	sbp150	dbp150	mbp150	hr150	sbp165	dbp165	mbp165	hr165	
84	80	101	66	73	87	100	65	78	86	107	68	78	85	104	68	77	83	124	72	85	83	114	67	77	87	113	71	81	82	115	68	78	80	111	70	80	79									
71	87	103	61	71	88	105	59	70	85	107	58	69	86	106	59	71	82	103	61	71	81	101	8	67	80	105	59	70	83	101	49	62	81													
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77	67	102	53	66	67	91	45	57	60	104	68	77	62	112	56	71	63	100	51	63	63	110	63	76	62	101	65	79	69																	
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78	88	101	65	79	90	104	68	77	91	116	78	86	87	117	70	82	86	114	59	72	85	114	59	72	85	129	77	90	85	126	71	85	87	134	72	88	89	143	87	99	83					
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69	90	115	49	71	84	106	48	67	82	97	54	68	83	83	66	71	84	98	53	68	89	87	55	65	90	108	76	86	72	106	56	72	74	106	60	75	75	110	52	71	80	108	62	77	84	
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75	99	114	66	78	98	117	61	74	97	121	53	70	98	116	78	88	99	103	64	73	100	119	87	94	98	119	63	77	97	120	65	79	100	124	69	83	100	127	65	81	99					
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69	74	104	56	67	75	105	50	63	77	103	49	60	86	117	74	81	87	126	81	87	87	116	67	79	85	124	79	90	78	119	71	82	85													
74	61	108	59	70	65	113	68	79	63	119	69	81	61	123	69	82	66	121	70	88	65	121	71	87	64	121	68	86	63	122	78	95	61													
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79	82	97	63	70	83	94	63	70	78	104	68	77	77	107	68	78	87	100	65	78	88	101	65	79	89	104	68	77	75	114	77	85	92	104	56	67	91	109	58	69	88	112	59	71	82	
66	86	103	64	73	83	107	76	79	84	106	65	78	84	101	65	80	83	94	63	70	67	104	68	77	76	103	58	68	72	103	60	68	85													
60	50	108	54	67	55	112	59	71	75	103	55	65	68	103	58	68	60	103	49	60	62	117	74	81	60	112	59	70	67																	
85	82	123	68	81	87	121	64	76	89	116	60	71	80	120	67	79	81	103	65	74	79	120	85	93	78	125	85	94	81																	
73	93	102	60	70	91	107	60	70	92	101	60	67	83	96	54	63	79	99	50	62	76	111	63	72	83	107	67	74	84	115	68	78	88	120	70	81	87									
63	89	99	62	70	88	96	54	63	87	91	58	66	89	107	60	70	90	105	61	71	91	106	60	71	93	103	61	69	87	105	60	70	89													
65	63	105	52	67	66	96	54	63	67	102	60	70	69	106	64	74	68	107	58	69	67	104	60	70	67	105	60	72	63	103	67	75	64	114	60	73	64									
74	65	109	67	77	65	104	66	75	60	99	64	72	61	97	56	67	61	103	65	74	63	107	68	79	62	105	70	79	65	109	65	76	63													
70	73	99	62	70	70	96	54	63	68	91	60	67	73	105	70	84	76	112	68	88	77	110	67	85	77	106	65	81	79	115	65	75	83													
64	76	97	56	66	79	99	65	73	81	95	60	67	83	116	77	86	74	117	60	75	70	121	63	76	73	126	66	80	73	120	65	80	77	124	70	83	75									
70	96	100	67	74	93	114	67	76	94	95	67	72	94	101	67	73	97	115	70	79	98	124	70	79	98	126	68	82	92	119	65	78	96	117	62	75	97									
78	83	96	53	63	85	104	56	67	86	106																																				

sbp180	dbp180	mbp180	hr180	2 seg reg - mins	durtn of analgn in mins	no of times vassopres sor-pnp	no of times vassopres or-eph	analgn reqd	shvrrng	nausea	vomiting	other side effects
				50	135	0	0	1	2	2	2	2
				30	120	0	0	1	2	2	2	2
				25	90	2	0	1	2	2	2	2
				20	90	7	0	1	2	2	2	2
				25	105	3	0	1	2	2	2	2
				40	120	1	1	1	2	2	2	2
				40	135	6	0	1	2	2	2	2
				25	105	0	4	1	1	1	2	2
				30	105	0	0	1	2	2	2	2
				30	150	0	0	1	2	1	1	2
				30	150	0	0	1	2	2	2	2
				40	150	4	0	1	2	1	2	2
110	66	80	86	40	180	2	0	1	2	2	2	2
				30	120	0	0	2	2	2	2	2
				30	135	0	0	1	2	2	2	2
				30	150	0	0	1	2	2	2	2
				30	90	2	0	1	2	2	2	2
				40	75	0	0	1	2	2	2	2
				30	105	0	0	1	1	2	2	2
				30	135	0	0	1	2	2	2	2
				30	120	0	0	1	2	2	2	2
				30	120	3	0	1	2	2	2	2
				25	105	1	2	1	2	2	2	2
				30	120	4	0	1	2	2	2	2
				40	120	1	0	1	2	2	2	2
				25	120	3	0	1	2	2	2	2
				30	180	3	0	1	2	2	2	2
114	67	97	80	30	180	1	0	1	2	2	2	2
117	74	81	84	30	180	0	3	1	2	2	2	2
				30	120	4	1	1	2	2	2	2
				25	105	6	0	1	1	2	2	2
				25	105	0	0	1	2	2	2	2
				25	135	5	0	2	2	2	2	2
				30	120	0	0	1	2	2	2	2
				30	135	3	0	1	2	2	2	2
				25	120	0	0	1	2	2	2	2
				30	120	4	0	2	2	2	2	2
				40	135	4	0	1	2	2	2	2
				30	120	0	0	1	1	2	2	2
				30	120	2	0	1	2	2	2	2
				40	120	0	0	1	2	2	2	2
				30	120	4	0	1	2	2	2	2
				20	60	0	0	1	2	2	2	2
				30	135	4	0	1	1	2	2	2
				30	120	2	4	1	2	2	2	2
				25	90	0	0	1	2	2	2	2
				20	75	0	0	1	1	2	2	2
				25	60	0	0	1	2	2	2	2
158	77	97	100	60	180	0	0	1	2	2	2	2
				30	90	5	2	1	2	2	2	2
				40	135	5	0	1	2	2	2	2
				30	105	0	0	1	2	2	2	2
				30	120	3	5	1	2	2	2	2
				40	105	0	0	2	2	2	2	2
				25	90	0	0	2	2	2	2	2
				40	135	1	0	1	2	2	2	2
				30	120	0	0	1	2	2	2	2
				30	120	0	0	1	2	2	2	2
				30	90	0	0	1	2	2	2	2
				40	120	4	0	1	2	2	2	2
				30	105	6	0	1	2	2	2	2
				40	135	1	0	1	2	2	2	2
				30	105	0	0	1	2	2	2	2
				40	90	3	0	1	2	2	2	2
				30	120	0	5	1	2	2	2	2